Title: Neonatal Septic Arthritis: A Systematic Review

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Abstract

Background: Septic arthritis is an uncommon condition in neonates. It is a serious disorder, especially because of the possibility of sequelae if not identified and treated early. Also, because of the rarity of this condition in neonates and the paucity of signs and symptoms, the diagnosis of septic arthritis is more difficult than in older children. The published literature is limited to case series, which is why the purpose of this systematic review is to provide a comprehensive summary of neonatal septic arthritis based on the existing literature. This study aims to identify the changing trends over time, specifically focusing on intravenous canulation as a major risk factor observed in our unit that sparked the undertaking of the study.

Method: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) guidelines were used. Three search engines were used for a total of 239 studies. Twenty-six studies were screened in full text.Sixteen articles underwent a quantitative analysis. Due to limited data and heterogenous reporting, the data were summarized descriptively.

Results: The total number of babies and joints studied was 307 and 313, respectively, of which the proportion of male babies was mentioned in 12 case series, accounting for 136 (228) (60% [42-71%]). The most common presenting symptoms were swelling at the involved joint, erythema, and decreased range of motion in variable order. The most common site of involvement was the hip joint (42%), followed by the knee joint (27%).Staphylococcus aureus (40%) was the most commonly cultured pathogen, followed by Klebsiella (18%). Antibiotics alone were reported in only 12% (38 babies) of the cases. Open surgery was performed on 16% of the 49 babies. The rest of the babies responded to joint aspiration and irrigation, with or without immobilization. Prompt laboratory and radiographic evaluations can help reduce delays in diagnosis and improve outcomes. Blood and tissue cultures are positive in most of the cases.Previous culture reports for the same unit will guide the addition of empirical antibiotics.

Conclusions: In our case series, the majority of the babies were premature. The most common joint involved is the hip joint. The most common underlying cause is sepsis and cathetarization. Intrvenous canulation is also a major risk factor because of the continuity of metaphysis and ephiphysial vessels. The most common presenting symptom is local signs. Unexplained fever and irritability make it better to look for a local examination of joints. Follow-up is mandatory, as a long-term sequel is more.

Keywords: Neonate, Sepsis, Septic arthritis, Knee joint

Introduction and Background

Septic arthritis is inflammation of the joints, secondary to an infectious aetiology that includes most commonly bacterial but can also be fungal, viral, or other pathogens (1). It is an uncommon condition in neonates, nonetheless a very serious one, mainly because babies can become permanent handicaps if not diagnosed and treated early (2). The important reason for the delayed diagnosis is the paucity of symptoms and signs in neonates (3). Osteoarticular infections in newborns are usually blood-borne infections (4,5). Neonates requiring NICU admission for prematurity, ventilator therapy, and invasive procedures are known to be predisposing actors, which are related to the risk of bacteremia (6).

The incidence of septic arthritis varies in different regions, such as 0.12/1000 live births in Singapore (5) and 1 in 1500 in India (7). Such a low rate of incidence indicates the difficulty of earlier diagnosis. Also, usual attention has been paid to neonatal septic arthritis of the lower limbs, especially the hip (8–13), but there are reports of involvement of the shoulder joint (14).

Staphylococcus aureus is the most prevalent organism involved in osteoarticular infections, the important reason being that the risk of this bacteremia rises with invasive procedures. However, there is an increasing trend of cases due to Klebsiella that have been reported (9–11, 15), a possible reason being contaminated equipment, which should alert the physicians for further cases. Other reported bacterial pathogens include Candida (16), Pseudomonas, Staphylococcus epidermidis, Streptococcus spp., Haemophilus influenza, Proteus, etc.

Neonatal septic arthritis is an uncommon condition and less reported; thereby, the purpose of this systematic review is to summarize the epidemiology, presenting symptoms, laboratory values, radiological inputs, microbiology, and treatment results of neonatal septic arthritis and to know the changing trends.

Review

Materials and methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol (PRISMA-P) guidelines were strictly followed. Additionally, the review was registered with PROSPERO CRD42021281293.

Search strategy

The literature search was performed by the authors using the following searches: Medical Subject Heading (MeSH) term: population, search fields: neonate; MeSH term: diagnosis, search fields: septic arthritis. PubMed, Scopus, Embase, and Ovid/Medical Literature Analysis and Retrieval System Online (MEDLINE) databases were used. Search fields were alternated until no new articles were revealed. At that point, the search was considered complete.

As is the truth, during neonatal periods and infancy, there is an anastomosis between joints and bone arteries that facilitates the transmission of bacterial infections from bone to joint and vice versa. So during neonatal periods and early infancy, in most cases, these infections are associated with osteoarthritis. Therefore, we included these two diseases.

Study Screening and Selection

The search yielded a total of 253 studies (Figure*1*). After the removal of duplicates, 239 articles remained. Based on the title and abstract review performed by all four authors, a total of 26 articles were included for qualitative review. The bibliographies of all articles reviewed were thoroughly evaluated to determine if any other relevant articles had been unintentionally overlooked. The independent full-text screenings of the articles were performed by all four authors. Of the 26 screened articles, 10 did not meet our inclusion/exclusion criteria (Table *1*). The resulting 16 articles underwent quantitative analysis. We incorporated all studies, regardless of their timeframe. We specifically included articles that were solely in the English language.

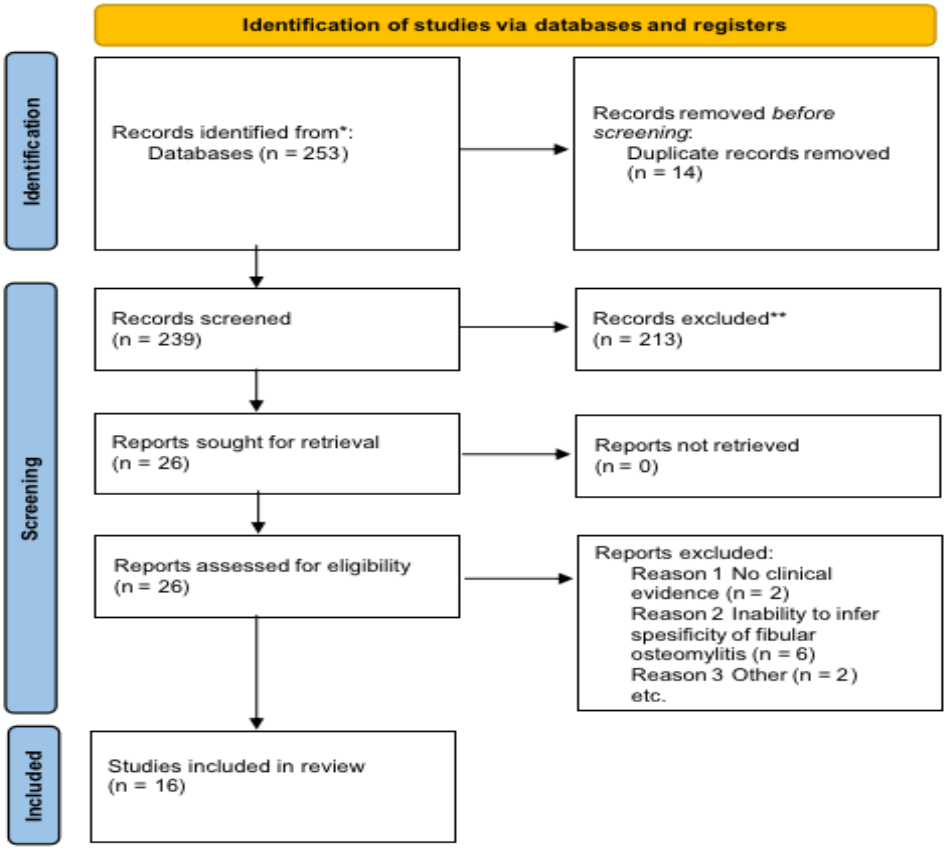

Figure 1: PRISMA flow diagram

TABLE 1: Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Onset of symptoms in neonatal period (< 28 days)	Level V evidence
The diagnosis of septic arthritis of an joint	The absence of at least one data table beyond the demographics
Level IV evidence or higher	Minimum follow-up of 3 months

Data Collection

The categories for data gathering included population demographics, gestational age, age of presentation, average birth weight, presence of risk factors such as prematurity, presenting features, number of joints involved, probable causative factors, laboratory values, imaging modalities, microbiologic diagnosis, medical management, surgical management, and complications. The variables included under demographic features were gestational age, emphasizing prematurity, age of presentation, and gender, with a mainly male predominance. The presenting features were recorded as binary variables.The C-reactive protein (CRP), leukocyte count, and initial temperature were recorded. The use and positive results of ultrasound (US), computed tomography (CT) and MRI were recorded. Joint involvement, aspirate, surgical and blood cultures as well as the disease course and hospitalization details were all documented. Duration of treatment including intravenous or oral antibiotics was noted; open versus US/CT-guided percutaneous drainage operations performed along with type/number also included in records. After follow-up completion, any secondary sequelae detected were accounted for accordingly.

Quality Assessment

To assess the included studies, which were predominantly case series, guidelines from the National Institutes of Health (NIH) were used (17).Since all the published literature is limited to a level of clinical evidence of IV, a quality assessment tool for case series under NIH was used. This tool has been modified to appropriately evaluate the methodologic quality of case series in light of their most common pitfalls. It includes a series of nine questions. According to the NIH Quality Assessment Tool for Case Series Studies, as described by Uthraraj et al. (2022) and Rubin et al. (2020), it was determined that these two studies fell into the poor quality category (6/9). On the other hand, Salamon et al. (2020), Yiqiang-li et al. (2016), and W. Khriesat et al. (2010) were classified as good quality studies (9/9). The remaining studies were classified as of fair quality (8/9).

Data Abstraction and Statistical Analysis

Due to heterogeneous data and a smaller sample size, we also included an extended time frame, which is why a meta-analysis could not be performed. All data were summarized descriptively according to the recommendations of Dhawan et al. (18). Frequencies and proportions were calculated for categorical variables. Means and standard deviations were calculated for continuous variables. Data abstraction and figure creation were performed with Microsoft Excel version 16.42.

Results

Demographic Features

Our review included 16 articles for a total of 307 neonates with involvement in 313 joints (Table 2). This review included neonates from all over the world, from 1976 to 2022.

Table 2 *Demography of case series*

		Country		Journal	Total patients	Total joints
1	Uthraraj et al(8)	India	2022	Cureus	14	16
2	Lorry G.Rubin et al(13)	United states	2020	The journal of pediatrics	45	23
3	Aneta Soltirovska Salamon et al(19)	Slovenia	2020	Signa Vitae	15	7
4	Sreenivas et al (9)	India	2016	Eur J Orthop Surg Traumatol	29	34
5	YiQiang Li et al(20)	China	2016	Medicine	52	56
6	Wadah Khriesat et al(10)	Jordan	2010	Journal of Pediatric Infectious disease	27	37
7	Kabak et al(2)	Turkey	2002	Pediatrics International	14	14
8	C.F.A. Bos et al(14)	The Netherlands	1998	The Journal of Bone and Joint Surgery	8	10
9	Merchant et al(16)	India	1997	Journal of Tropical Pediatrics	8	8
10	Dinesh Halder et al(6)	Malaysia	1996	Southeast Asian Journal of Tropical Medicine	10	14
11	Abuekteish et al(11)	Jordan	1995	Eur J Pediatr	17	20
12	Vidigal et al(12)	Brazil	1993	International Orthopaedics	14	14
13	Adeyemo et al(15)	Nigeria	1993	Annals of Tropical Paediatrics	12	23
14	Frederiksen et al(21)	Denmark	1992	European Journal of Pediatrics	22	7
15	N K Ho et al(5)	Singapore	1989	Singapore Medicine Journal	11	21
16	Pittard III et al (22)	America	1976	The Journal of Pediatrics	9	9

It included neonates with a prematurity (<37 weeks) proportion of 66% (7-100%). 12 case series mentioned the gender proportion, of which males comprised 136/228 cases (60%), and females comprised 92/228 cases (40%). (Table 3) The age of onset of symptoms was predominantly in the 3rd week, at an average of 20 days (8–40 days).

Joints involved

The most common site of involvement was the hip joint (42%), followed by the knee joint (27%).

Table 3 *Patient details*

		DOL of symptoms	**Birthweight (Average)**	**Prematurity**	**Male %**	**Most common joint**
1	Uthraraj et al (8)	8	1800gm	8 (57%)	6(43%)	Hip (14)
2	Lorry G.Rubin et al (13)	30	1040gm	39 (87%)	NR	Knee (14) > Hip (9)
3	Aneta Soltirovska Salamon et al (19)	19	3670gm	none	9(60%)	shoulder(3) > Hip (2)
4	Sreenivas et al (9)	23+4	NR	20 (69%)	12(42%)	Hip (14) > Knee (2)
5	YiQiang Li et al (20)	17+6	3010gm	7 (13.5%)	37(71%)	Knee (22) > Hip (13)
6	Wadah Khriesat et al (10)	12-33	2915+935gm	13 (48%)	15(56%)	Hip(19)
7	Kabak et al (2)	34	2450gm	4 (29%)	9(64%)	hip(6) > knee (5)
8	C.F.A. Bos et al (14)	NR	NR	2(25%)	NR	shoulder (8)
9	Merchant et al (16)	26+11	1310gm	8 (100%)	NR	Knee(15)
10	Dinesh Halder et al (6)	15.6	1430	9 (90%)	6(60%)	Knee(9)
11	Abuekteish et al (11)	19	2500	9 (53%)	11 (67%)	Hip (17)
12	Vidigal et al (12)	17	2500	1 (7%)	NR	Hip (14)
13	Adeyemo et al (15)	17	2200	3 (25%)	5 (42%)	Hip (12)
14	Frederiksen et al (21)	<40 days	1765	13 (59%)	14(64%)	Hip (7)
15	N K Ho et al (5)	20-40	2270	6 (55%)	6 (55%)	Knee (10) > Hip (6)
16	Pittard III et al (22)	22	2106	6 (67%)	6 (67%)	Knee (9)

Presenting symptoms

As mentioned earlier, the paucity of signs and symptoms is one of the important reasons for the delayed diagnosis of septic arthritis. Similarly, the presence of initial symptoms was vague and less reported, which included fever and irritability. However, most of the neonates presented with joint swelling, tenderness, erythema, and a reduced range of movements of the affected joint, with or without pseudoparalysis, in variable order (Table 4).

Underlying causes

The most important cause documented is NICU admission, with the reasons being respiratory distress syndrome, sepsis, and birth asphyxia (Table 4). Umbilical catheterization has been a documented risk factor in 36 cases in 4 case series.

Microbiology

Staphylococcus aureus (40%) was the most commonly cultured pathogen, followed by Klebsiella (18%). 1 case series, which included 8, exclusively reported the cases of Candida. Other microorganisms reported were Pseudomonas, Streptococcus, H. influenzae, Staph hemolyticus, Escherichia coli, Proteus, etc.

Table 4 *Presenting symptoms*

		Underlying causes	Clinical features	Organism
1	Uthraraj et al (8)	RDS(5) Sepsis(5) Birth asphyxia(3)	Reduced active joint movements Raised temperature	Pseudomonas (56%) Klebsiella pneumonia (25%) MS - Staphlococcus aureus (19%)
2	Lorry G.Rubin et al (13)	Total parenteral nutrition (25) Sepsis Central venous catheterisation(1)	Swelling(64%) Erythema(56%) Reduced movement (22%)	Staphylococcus (MSSA > MRSA)
3	Aneta Soltirovska Salamon et al (19)	Sepsis Umbilical catheterisation (1)	Irritability and feed intolerance Limited range of motion (87%) Limb pain and swelling (75%)	staph aureus >streptococcus agalactiae > escherichia coli
4	Sreenivas et al (9)	Sepsis Birth asphyxia (16)	Pseudoparalysis (69%) Swelling (79%)	klebsiella pneumonia > Staph aureus
5	YiQiang Li	Sepsis	Pseudoparesis (50%)	Staph aureus >

	et al (20)		Swelling (13.5%)	Klebsiella
6	Wadah Khriesat et al (10)	NICU admission Umbilical catheterisation(6)	NR	klebsiella pneumonia > staph aureus > enterobacter
7	Kabak et al (2)	Sepsis	Swelling/erythema/decreased range of motion	Staph aureus > Staph epidermidis
8	C.F.A. Bos et al (14)	NICU admission	Swelling,pyrexia, inability to use involved arm	Staph.aureus > H.influenza
9	Merchant et al (16)	Sepsis (Candidiasis)	Tender swelling of involved joint	Candida
10	Dinesh Halder et al (6)	Umbilical catheterisation (6)	Swelling (100%) Tenderness(90%) Limited movement (60%)	MRSA > Klebsiella
11	Abuekteish et al (11)	Sepsis	Joint tenderness, swelling, Limitation of joint movement	Klebsiella > Staph aureus
12	Vidigal et al (12)	Sepsis	Joint tenderness, pain of movement, Pseudo paralysis	Staphlococcus aureus > Staph albus> Staph hemolyticus
13	Adeyemo et al (15)	Perinatal asphyxia (7) Sepsis	Local tenderness, swelling, Limitation of movements	Klebsiella (12), Staph aureus > Candida
14	Frederiksen et al (210	UAC (15) RDS(15) Birth asphyxia (10)	Pseudoparalysis, soft tissue swelling	staph aureus
15	N K Ho et al (5)	UVC catheter(8) Sepsis (9) meningitis	Joint swelling, tenderness	Staph aureus > Candida
16	Pittard III et al (22)	RDS, Birth Asphyxia, Sepsis	Swelling, tenderness, abnormal positioning of affected leg	Staph aureus > Candida

Laboratory Assessment

The blood parameters usually assessed in cases of osteartícular infections are WBC count, ESR, and CRP (Table 5). In the reported case series, CRP and ESR are elevated. The WBC count also showed variability, with five case series showing a normal range and seven case series showing elevated levels. Like the literature says, elevated inflammatory markers are not always necessary in cases of

septic arthritis.

Imaging

Earlier case series studies in this review mainly used radiographs as the modality of imaging (Table 5). The important findings were radiological changes in epiphysis and metaphysis, soft tissue swelling, bone lesions, periosteal bone formation, joint dislocation, or subluxation, in variable order and depending on the day of diagnosis. Subsequently, USG has become the imaging modality, where findings include joint effusion, thickened periosteum, thickened synovium, elevated synovium, and subperiosteal abscess. MRI was done in two case series, where findings included bone marrow edema,periosteal reaction, and joint effusion.

Table 5 *Investigations*

		CRP/ESR	WBC	X Ray findings	USG findings
1	Uthraraj et al (8)	Elevated (100%)	Elevated > 20000 (100%)	-	Fluid pockets > 7x11mm mri-bone marrow edema,periosteal reaction,joint effusion
2	Lorry G.Rubin et al (13)	NR	18200 cells	periosteal reactions,lytic lesion,joint swelling or effusion	no fluid,simple effusion,complex effusion, MRI - metaphyseal involvement,subperiosteal abscess
3	Aneta Soltirovska Salamon et al (19)	Elevated (87%)	NR	osteolytic lesions, soft tissue edema, periosteal reaction	joint effusion,thickened periosteum,thickened synovium,elevated synovium,sub periosteal abscess
4	Sreenivas et al (9)	NR	Elevated (100%)	-	effussion/subperiosteal abcess,positive 22(75.9%),negative 7(14.1%)
5	YiQiang Li et al (20)	NR	Elevated (75%)	Joint dislocation or subluxation, Damage to metaphysis or epiphysis	-
6	Wadah Khriesat et al (10)	28.5+17 mg/dl ESR 55+16	Elevated (15%)	-	-
7	Kabak et al (2)	52.6 mg/dl ESR 68.9 mm/h	>12000 cells/mm3	Widening of joint space, Swelling of soft tissue	Synovial effusion
8	C.F.A. Bos et al (14)	NR	Normal range	Radiological changes in epiphysis and metaphysis	-
9	Merchant et	NR	Normal	Soft tissue	-

	al (16)		range	swelling – changes of metaphysitis	
10	Dinesh Halder et al (6)	NR	~19000cells/mm3	Soft tissue swelling(90%) Bone lesions(60%) Periosteal bone formation(10%)	-
11	Abuekteish et al (11)	ESR high (42-137mm/h)	Normal range	Periosteal reaction or lytic lesion	-
12	Vidigal et al (12)	NR	Normal range	Subluxation/Pathological dislocation of hip	
13	Adeyemo et al (15)	NR	soft tissue swelling, widened joint space, increased bone density, periosteal elevation and osteomyletic lesions		
14	Frederiksen et al (21)	Normal range	Normal range	Soft tissue swelling followed by periosteal new bone formation	
15	N K Ho et al (5)	NR	NR	-	-
16	Pittard III et al (22)	NR	Not consistent >25000 (3) <12000(3)	Soft tissue swelling/Sno vial thickening/Small effusion	

Medical Management

The mean duration of IV followed by oral antibiotics was 2–6 weeks. Antibiotics alone were reported in only 12% (38 babies) of the cases.

Surgical Management

Open surgery i.e., a throtomy was performed on 16% of the 49 babies. The rest of the babies responded to joint aspiration and irrigation, with or without immobilization (Table 6).

Complications or Sequelae

Five case series were documented to have no sequelae on follow-up (Table 6), which cited early diagnosis and prompt management as the reasons for this result. The rest of the case series included limb length discrepancy as the most common complication, a possible reason being joint subluxation, dislocation, or avascular necrosis of the femoral head. (Table 6)

Table 6 *Treatment and sequelae*

		Antibiotics	**Surgical Management**	**Complications/sequelae**
1	Uthraraj et al (8)	Amoxicillin with clavunate	Arthrotomy	No sequelae
2	Lorry G.Rubin et al (13)	Nafcillin/oxacillin,cefazolin, vancomycin,rifampin	drainage of joint and bone	Limb length discrepancy (3) Elbow deformity (1) Knee deformity(1)
3	Aneta Soltirovska Salamon et al (19)	cefotaxime,flucloxacillin,	drainage of pus,and irrigation of affected bone/joint	No sequelae
4	Sreenivas et al (9)	ceftriaxone ,gentamcin	emergency arthrotomy,joint lavage	Hip dislocation (5)
5	YiQiang Li et al (20)	Cephalosporin + Clindamycin based on sensitivity reports (2+2)	Open surgical drainage(72%)	Avasular necrosis of femoral head(6) Joint dislocation (4)
6	Wadah Khriesat et al (10)	imepenem,vancomycin (4-6 weeks)	Irrigation, drainage and immobilisation (4-6wk)	NR
7	Kabak et al (2)	Antistaphylococcal drugs (3-4 weeks)	Irrigation, drainage and immobilisation (4-6wk)	Hip subluxation and destruction of

				femoral head (1)
8	C.F.A. Bos et al (14)	NR (8-14 weeks)	NR	Shortening of limbs (3)
9	Merchant et al (16)	Fluconazole (3 weeks)	NR	No sequelae
10	Dinesh Halder et al (6)	Cephalosporin/Clindamycin/Vancomycin	NR	Abnormal joint function and growth (1)
11	Abuekteish et al (11)	Nafcillin/oxacillin	surgical drainage procedure (42%)	No sequelae
12	Vidigal et al (12)	NR	Arthrotomy	Limp(5), limited movements , pathological dislocation
13	Adeyemo et al (15)	cloxacillin,gentamicin,	NR	Unstable hip joint with shortening of limb
14	Frederiksen et al (21)	dicloxacillin,methicillin, gentamicin,benzyl penicillin,	joint aspiration	Sequelae (4) Subluxation, displacement, femoral head destruction
15	N K Ho et al (5)	NR	Joint aspiration	Shortening of limbs No sequelae(1)
16	Pittard III et al (22)	Methicillin,Ampicillin, Gentamycin Amphotericin	NR	Full recovery

NR:Not Reported

Discussion

Our review included 16 articles for a total of 307 neonates with involvement of 313 joints. It included neonates with a prematurity (< 37 weeks) proportion of 66% (7-100%). These details are in concordance with Kleinman et al., who demonstrated that preterm and low birth weight infants are 3-10 times more likely to develop septic arthritis 12 case series mentioned the gender proportion of which Males comprised 136/228 cases (60%), and females comprised92/228 (40%), immunological differences in gender may explain above findings. The age of onset of symptoms was predominantly in the 3rd week, at an average of 20 days (8-40 days). The delayed presentation explained by low immunity in the preterm neonate to cause inflammation and late-onset sepsis catheterisation and hospital admissions were the major risk factors (23).

The presence of initial symptoms was vague and less reported, which included fever and irritability. Fever, even though considered common in septic arthritis, is difficult to document in neonates because of physiological neonatal hypothermia (24). This review emphasizes the importance of susceptibility to septic arthritis with the above signs. However, most of the neonates presented with joint swelling, tenderness, erythema, and a reduced range of movements of the affected joint, with or without pseudoparalysis, in variable order. The most important cause documented is NICU admission, with the reasons being respiratory distress syndrome, sepsis, and birth asphyxia.

Umbilical catheterization has been a documented risk factor in 36 cases in 4 case series (2, 5, 6, 19) Diagnosis is difficult (25). Kabak S. et al. mentioned that intravenous canulation (3/14) is a risk factor for septic arthritis(2). Bergdahl S. and Woong M. also reported that intravenous canulation is a major risk factor. In our study, intravenous canulation-induced septic arthritis was not uncommon(26,27).

In the reported case series, CRP and ESR are elevated. The WBC count also showed variability, with 5 cases showing a normal range and 7 cases showing elevated levels. Thus, measuring both ESR and CRP may slightly improve sensitivity and negative predictive value for diagnosis; however, further investigation is necessary to establish a certain diagnostic role in septic arthritis. In our review, most of the cases were not reported. In some cases, they were also normal.

The important findings in radiographs were changes in epiphysis and metaphysis, soft tissue swelling, bone lesions, periosteal bone formation, joint dislocation, or subluxation, in variable order and depending on the day of diagnosis. Subsequently, USG has become the imaging modality, where findings include joint effusion, thickened periosteum, thickened synovium, elevated synovium, and

subperiosteal abscess. MRI was done in 7 patients in 2 case series (13, 19), where findings included bone marrow oedema, periosteal reaction, and joint effusion. This is to emphasize that imaging plays a crucial role in establishing early and timely diagnosis, which is subsequently helpful in management, thus decreasing the incidence of long-term sequelae (19).

Staphylococcus aureus (40%) was the most commonly cultured pathogen, followed by Klebsiella (18%). One case series, which included 8 cases, exclusively reported the cases of Candida (16). Other microorganisms reported were Pseudomonas (8), Streptococcus, and Staph. hemolyticus, H. influenzae, Staph. hemolyticus, Escherichia coli, Proteus, etc. This is in concordance with published literature (28). An increase in methicillin-resistant S. aureus (MRSA) has been reported in the pediatric population and should always be considered when deciding on empiric antimicrobial treatment. Four of the reviewed case series (9–11, 15) highlighted the increasing incidence of Klebsiella-related septic arthritis, citing the possibility of using contaminated equipment (29), which is an important reason for nosocomial infection. Another reason noted was a severe shortage of water supply (15), which, when corrected, led to no recurrence of this infection. Pseudomonas reported in Uthraraj et al. (8) was important because of its nosocomial nature. The main cause of this outbreak was inadequate infection control by staff members. Thus, guidelines formulated to mitigate the risk lead to no further outbreak (8). Haemophilus influenzae was cultured in only one case (14), which is consistent with the drastic decrease in the cases of osteomyelitis secondary to H. influenzae after the introduction of large-scale vaccinations (27). The culture and identification of the offending pathogen allow for definitive therapy with a narrow spectrum representing the cost-effective and responsible use of antibiotic resources (29).

Administration of antibiotics alone was reported in only 12% (38 babies) of the cases. Initial choices were mainly anti-staphylococcal drugs with a combination of aminoglycosides, followed by cephalosporins. Also for fungal arthritis, fluconazole was effective (16); however, amphotericin was helpful in another case series (22). Open surgery was performed in 16% (49 babies). The rest of the babies responded to joint aspiration and irrigation, with or without immobilization.

There is still no consensus of opinion as regards the management of septic arthritis, let alone neonatal arthritis. Some advocate arthrotomy (8, 9, 11, 12, 20), while others prefer aspiration of infected joints (2, 10, 13, 19, 21, 22).In general, conservative therapy was elected in small premature infants, while a surgical approach is done in newborns with larger joints (22). Another discussion to decide on the choice of therapy based on the site of pus detection. If the pus is superficial and swelling

is easily visible and monitored, repeated careful aspirations are the preferred method for decompression, and when it is deep-seated, especially in hip joints, an arthrotomy is the preferred method (5).

The importance of this review lies in the fact that an early diagnosis and appropriate management would decrease the incidence of sequelae in newborn babies with septic arthritis. 5 case series are documented to have no sequelae on follow-up (8, 11, 16, 19, 22). The rest of the case series included limb length discrepancy as the most common complication, a possible reason being a joint subluxation, dislocation, or avascular necrosis of the femoral head. This is also seen in septic arthritis of the shoulder joint (14).It is worth mentioning here that, according to Diana V et al., infants with lupus may have weakened immunity, making them more vulnerable to septic arthritis(30). Parmar J et al. reported a case of a 5-week-old baby presenting with septic arthritis in the knee and TMJ believed to be caused by omphalitis (31).
This study is not without its limitations. Due to the rarity of neonatal septic arthritis, this systematic review was limited to case series and is thus of level IV evidence. Due to heterogeneous data and variable follow-up, we are limited in the interpretation of our data about presenting symptoms, choice of treatment, and complications, so we are unable *to do a meta-analysis. The follow-up period was very short in comparison. Some studies were in single numbers. The time frame of the studies was very wide. Only three studies were of good quality.*

Conclusions

Unexplained fever and irritability in a newborn with a significant NICU course should raise suspicion of neonatal sepic arthritis, which, on examination, if associated with any joint swelling, tenderness, or decreased range of movements, should be advised for further radiographic evaluation.Though laboratory screening tests may be normal, radiographs can help reduce the delay in diagnosis and improve outcomes. For focused treatment,blood and tissue cultures are to beperformed.A prolonged stay is a major concern as it may involve invasive procedures like simple intravenous cannula insertion.Improvements in our microbiological diagnosis have the potential to improve antibiotic selection. Local MRSAprevalence must be taken into consideration when starting empiric antibiotic treatment.Follwup is a must, as complications are common in delayed cases.

Additional Information

Disclosures

Conflicts of interest: In *compliance* with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous

three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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